UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/310,667	05/12/1999	DAVID J. ECKER	IBIS-0012	9164

34138 7590 01/30/2004

COZEN O'CONNOR, P.C.
1900 MARKET STREET
PHILADELPHIA, PA 19103-3508

EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/310,667	ECKER ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on th cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-29,35-41 and 43-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-29,35-41 and 43-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *01 May 2003* is: a)☐ approved b)☒ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/2003* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on October 1, 2003 has been entered. The claims pending in this application are claims 27-29, 35-41, and 43-67. Rejection and/ or objection not reiterated from the previous office action are hereby withdrawn in view of the amendment filed on October 1, 2003. The following rejections are based on amendment.

Drawings

2. The corrected drawings submitted on May 1, 2003 have been disapproved because they introduce new matter into the drawings. 37 CFR 1.121(a)(6) states that no amendment may introduce new matter into the disclosure of an application. The added or deleted materials in Figures 4 and 5A which are not supported by the original disclosure is as follows:

(1) in the corrected Figure 4, there is no connection between "Annotations Relational Database" and "Filter & Sort" which is shown in original filed Figure 4. Furthermore, the meaning "

Response to Arguments

In page 16, last paragraph bridging to page 17, third paragraph of applicant's remarks, applicant argues that "Figure 4 describes a flow-scheme for the QC Compare protocol which must use the Blast database and the Annotation database of Figure 3. The concept of 'Annotations Relational Database' presented in Figure 4 finds support in the original disclosure at page 20, line 10 and page 21, lines 5-6. 'Annotations Relational Database' also appears at bottom of Figure 3, and it is implied that the information of Figure 4 flows from the information presented at the

bottom of Figure 3 immediately preceding Figure 4; thus, Annotations Relational Database was part of the application as filed and is therefore not new matter. The informal drawing originally submitted showed a two column format to indicate two streams of input into 'filter & Sort' where the connection between Annotations Relational Database and Filter & Sort was assumed. In the formal drawings submitted on May 1, 2003, a formal drawing was submitted for Figure 4. in which 'parsed Annotations' was amended to 'Annotations Relational Database' and the connecting line was included in order to more particular describe the connection between Figure 3 and Figure 4, and more particular describe the claimed invention. Furthermore, according to Webster's Revised Unabridged Dictionary (1913), to parse means 'to resolve intc its elements, as a sentence, pointing out the several parts of speech, and their relation to each other by government or agreement' Therefore, Annotations Relational Database and Parsed Annotations have the same meaning in the context of Figure 4. Thus, no new matter was added to Figure 4.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, the support for "Annotations Relational Database" can not find in the in the original disclosure at page 20, line 10 and page 21, lines 5-6 as suggested by applicant. Since the specification contains several different specifications, applicant is required to specifically indicate which specification he is used for the argument. Second, the examiner noted that, in amended Figure 4, "parsed Annotations" was amended to 'Annotations Relational Database". However, there is no connecting line between "Annotations Relational Database" and "Filter & Sort"in the amended Figure 4 filed on May 1, 2003, which is different from what

applicant suggests. Third, since applicant has amended "parsed Annotations" to 'Annotations Relational Database", whether Annotations Relational Database and Parsed Annotations have the same meaning is not an issue for the arguments.

(2) in the corrected Figure 5A, "Is Weighted Percent of Matches at Point in Compare Better than Corresponding Point in bestArray?" in original filed Figure 5A is replaced with "Weighted Percent of Matches at better than corresponding point in bestArray? The meanings of two phrases are different.

(3) in the corrected Figure 5A, "Set Point in bestArray to Weighted Match Percent" in original filed Figure 5A is replaced with "Set Point in bestArray =Weighted Match%". The meanings of two phrases are different.

Applicant is required to cancel these new matters in the reply to this Office Action.

Response to Arguments

In page 17, second and third paragraphs of applicant's remarks, applicant argues that: (1) "[F]igure 5A is a flow chart describing the logical analysis and pathway of preferred steps in the CompareOverWins algorithm. Support for the figure as amended can be found at page 23, line 2 and in Example 2 on page 35, lines 11-15 of the original disclosure. The diamond-shaped box represents a 'yes' or 'no' decision point in the process, and the question asked is found within the diamond. In this context, the original phrase 'Is Weighted Percent of Matches at better than in bestArray?' and the amended phrase 'is Weighted Percent of Matches better than Corresponding Point in bestarray?' have the same meaning and provoke the same 'yes' or 'no'

decision"; and (2)the phrase "Set Point in bestArray to Weighted Match Percent" in original filed Figure 5A and the phrase "Set Point in bestArray =Weighted Match%" in amended Figure 5A filed on May 1, 2003 has the same meanings since "the phrases are written as imperative commands, where the word 'to' is equivalent to "equal to" which is equivalent to the symbol '=' and the word 'Percent' is equivalent to the symbol '%'.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, applicant does not explain why the original phrase "Is Weighted Percent of Matches at better than in bestArray?" and the amended phrase "is Weighted Percent of Matches better than Corresponding Point in bestarray?" have the same meaning. From plain meaning, it is obviously that two phrases have different meaning. Second, the examiner agrees that the word "Percent" is equivalent to the symbol "%". However, the examiner does not agree that the word "to" and the phrase "equal to" have the same plain meaning since the dictionary does not indicate that the word "to" is equivalent to the phrase " equal to". Third, if applicant believes that these amended phrases do not change meanings of Figure 5A, this is no sense to make these changes in Figure 5A.

Specification

3. The substitute specification filed on October 1, 2003 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because applicant does not provide a maked up version of the substitute specification.

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. For example, see ncbi.nlm.nih.gov/Omim/. CGAP in page 12, line 1 of the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Response to Arguments

In page 18, first paragraph of applicant's remarks, applicant argues "[T]he present specification has been amended so as to delete all hyperllnk and/or other form of browser-executable code".

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because the substitute specification filed on October 1, 2003 has not been entered.

5. The disclosure is objected to because of the following informality: applicant is required to update priority information for US application 09/760,440 in the first sentence of the specification (substituted specification) filed on October 21, 2002 since US application 09/760,440 now is US patent No. 6,221,587.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 27-29, 35-41, and 43-67 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 27-29, 35-41, and 43-67 as written, do not sufficiently distinguish over naturally nucleic acids because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

Claim Rejections - 35 U.S.C. § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode by the inventor of carrying out his invention.

8. Claims 27-29, 35-41, and 43-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although the specification describes iron response element and 3' untranslated region of the histone mRNA (see specification, pages 32-38), the specification does not adequately describe that: (1) an oligonucleotide comprising a molecular interaction site that is present in the RNA

does not comprise the iron response element in claims 35-41 and 43-51; (2) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element or the 3' untranslated region of the histone mRNA in claims 52-67; and (3) the binding of said molecule to said molecular interaction site does not modulate translation of said RNA as recited in claims 27-29. MPEP 2163.06 states that "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." In view of the embodiments adequately description in the specification, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of the full scopes of products encompass in the claims at the time of the application was filled. Therefore, the written description requirement has not been satisfied.

In support of this position, attention is directed to the decision of *Vas-Cath inc. V. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 U.S.C. 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

9. Claims 27-29, 35-41, and 43-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp.71427-71440.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The specification (for example, see page 32-44) provides adequate written descriptions for iron response element in 5' untranslated region of ferritin mRNA and in 3' untranslated region of transferrin receptor mRNA, 3' untranslated regions of histone and vimentin mRNAs, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4. However, the specification fails to adequately describe: (1) any kind of oligonucleotide comprising a molecular interaction site in RNA of a selected organism and in RNA of at least one additional organism wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular interaction site modulates the expression of said RNA in said selected organism and wherein said oligonucleotide does not comprise an iron response element as recited in claims 35-41 and 43-67; and (2) any kind of oligonucleotide comprising a molecular interaction site that is present in prokaryotic RNA and in at least one additional prokaryotic RNA wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular

interaction site modulates the expression of said prokaryotic RNA and wherein the binding of said molecule to said molecular interaction site does not modulate translation of said RNA as recited in claims 27-29. The claimed inventions as a whole are not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed inventions as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

In this instant case, in view of the teachings in the specification, claims 35, 51, 52, and 67 are read as any kind of oligonucleotide comprising a molecular interaction site in RNA of a selected organism and in RNA of at least one additional organism wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular interaction site modulates the expression of said RNA in said selected organism and wherein said oligonucleotide does not comprise an iron response element. Claim 27 is read as any kind of oligonucleotide comprising a molecular interaction site that is present in prokaryotic RNA and in at least one additional prokaryotic RNA, wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular interaction site modulates the expression of said prokaryotic RNA and wherein the binding of said molecule to said molecular interaction site does not modulate translation of said

RNA. Since independent claims 35, 51, 52, and 67 are directed to a product and are not directed to a method and it is well established that the determination of the patentability of the product is based on the product itself and is not dependent on the method for identifying the product, the method as recited in claims 35, 51, 52, and 67 is not read into claims. Since it is known in the art that iron response elements from ferritin mRNAs from different species and human transferrin receptor have a highly conserved six-membered loop (Harrison *et al.*,Biochim. Biophys. Acta, 1275, 161-203, 1996, see page 186, Figure 12) and a sequence of 28 nucleotides within putative stem-loops in the 5'-UTR of H- and L-ferritin mRNA of human, bullfrog, chicken, rabbit and the somal ferritin of the snail *Lymnaea stagnalis* as well as in rat is highly conserved and this sequence has been demonstrated to be essential (and sufficient) for the translational response to iron (Harrison *et al.*,Biochim. Biophys. Acta, 1275, 161-203, 1996, see page 187, right column, first paragraph), iron response element is an oligonucleotide comprising a molecular interaction site in RNA of a selected organism and in RNA of at least one additional organism wherein said molecular interaction site serves as a binding site for at least one molecule (ie., iron) and wherein binding of said molecule to said molecular interaction site modulates the expression of said RNA in said selected organism. Since the specification defines "Modulation" as "augmenting or diminishing RNA activity or expression" (see the specification, page 10, last paragraph), a well known "Shine & Dalgarno" sequence that is present in mRNAs from different bacteria can not considered as a molecular interaction site as recited in claims 27-29 since "Shine & Dalgarno" sequence does not augment or diminish RNA activity or expression (also see applicant's remarks, page 5, first paragraph). Although the specification adequately describes 3' untranslated regions

of histone and vimentin mRNAs and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4, the specification does not adequately describe whether a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can be considered as a molecular interaction site since there is no evidence to show that binding of a molecule to a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can modulate the expression of said RNAs in said organisms. In view of the teachings in the specification, besides iron response element, the specification does not describe other oligonucleotides comprising a molecular interaction site as recited in claims 27-29, 35-41, and 43-67. Therefore, claims 27-29, 35-41, and 43-67 encompass numerous unknown and unidentified oligonucleotides that miss from the disclosure. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

With limited disclosure provided by the specification, the skilled artisan cannot envision all oligonucleotides recited in claims 27-29, 35-41, and 43-67 and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co.* Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only iron response element meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Response to Arguments

I. In page 18, second paragraph bridging to page 20, first paragraph of applicant's remarks, applicant argues "the Applicants' claimed invention describes not solely the method, but also presents detailed description of structural elements such as nucleic acid sequences conserved between multiple organisms and stemloops which are predicted to be indicative of molecular interaction sites, and further provides examples of structures identified by the method which validate the ability of the method to identify the structures. For example, the specification discloses the iron response element (original specification, page 29, lines 3-5, and Example 1) and the Examiner acknowledges that 'Since it is known in the art that iron response elements from ferritin mRNAs from different species and human transferrin receptor have a highly conserved six-membered loop...and that this sequence has been demonstrated to be essential (and sufficient) for the 'translational response to iron..., iron response element is an oligonucleotide comprising a molecular interaction site...'(reference omitted; Office action, July 1, 2003, page 6, lines 8-1 7). Thus, the specification cites art recognized correlation between the identification of a structure

within a molecular interaction site of the invention and the modulation of its function. Additionally, in a previous Office Action mailed June 20, 2002, the examiner cites Manzella *et al.*, (J. Biol. Chem., 267, 7077-7082, 1992) and acknowledges that 'although Manzella *et al.*, did not directly disclose that modulation of the expression of ornithine decarboxylase mRNA by binding of a protein [sic] cytoplasmic extracts to ornithine decarboxylase mRNA 5'-UTR..., in the absence of convincing evidence to the contrary, this limitation was considered to be an inherent property" (Office action, June 20, 2002. page 8, lines 19-21 and bridging to page 9, line 1). Thus, the invention is not described solely in terms of the method used to identify the 'molecular interaction sites... wherein the molecular interaction site serves as a binding site for at least one molecule which, when bound to the molecular interaction site, modulates the expression of the RNA in the selected organism,' but also presents an example, ie., Example 1, describing an 'art recognized correlation or relationship between the structure of the invention and its function.'."

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, the claimed invention is directed to a product and is not directed to a method which is suggested by applicant. Second, the examiner agrees with applicant that the specification describes iron response element. Since iron response element is not part of limitations of claims 35-41 and 43-67, iron response element can not be considered as one of numerous unknown and unidentified oligonucleotides that miss from the disclosure. Third, since in view of applicant's response filed on March 17, 2003, the examiner has withdraw 102 (b) rejection based on Manzella *et al.*, the reference of Manzella *et al.*, is not an issue for the argument.

II. In page 20, second paragraph bridging to page 23, first paragraph of applicant's remarks, applicant argues "[A]pplicants' specification adequately discloses the claimed oligonucleotides comprising molecular interaction sites, and in doing so, also adequately describes relevant identifying characteristics of the molecular interaction sites." since (1) based on a known sequence, paralogs alignment can be used to identify the claimed olignucleotides comprising molecular interaction sites; and (2) "[A]pplicants have provided sufficient written description of 1) a representive number of species (for example, the iron response element, 3'-UTR of vimentin and 3'-UTR of histone mRNA), 2) reduction to drawings (Table 1 and Figures 31 and 38 for example) and 3) relevant, identifying characteristics of the claimed invention. Thus, not all oligonucleotides need be envisioned; a representative number of species of said genus are adequately described."; (3) "a patent applicant's disclosure, which contains a teaching of how to make and use the invention, must be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure"; and (4) the absence of working examples should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement, and the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, applicant argues that based on a known sequence, paralogs alignment can be used to identify the claimed olignucleotides comprising molecular interaction sites and one skilled in the art will be able to practice it without an undue amount of

experimentation in view of the specification. However, this argument is not persuasive because the rejection is based on lack of written description and is not based on lack of enablement. Second, since the specification defines "Modulation" as "augmenting or diminishing RNA activity or expression" (see the specification, page 10, last paragraph), a well known "Shine & Dalgarno" sequence that is present in mRNAs from different bacteria can not considered as a molecular interaction site as recited in claims 27-29 because "Shine & Dalgarno" sequence does not augment or diminish RNA activity or expression (also see applicant's remarks, page 5, first paragraph). Although the specification adequately describes 3' untranslated regions of histone and vimentin mRNAs and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4, the specification does not adequately describe whether a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can be considered as a molecular interaction site since there is no evidence to show that binding of a molecule to a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can modulate the expression of said RNAs in said organisms. In view of the teachings in the specification, besides iron response element, the specification does not describe other oligonucleotides comprising a molecular interaction site as recited in claims 27-29, 35-41, and 43-67. Therefore, claims 27-29, 35-41, and 43-67 encompass numerous unknown and unidentified oligonucleotides that miss from the disclosure. The general knowledge and level of skill in the art

do not supplement the omitted description because specific, not general, guidance is what is needed.

10. Claims 27-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that binding of one molecule to a molecular interaction site of a prokaryotic RNA only can modulate the expression of said prokaryotic RNA but can not modulate translation of said RNA. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability why binding of one molecule to a molecular interaction site of a prokaryotic RNA, which can modulate the expression of said prokaryotic RNA, can not modulate translation of said RNA.

Claims 27-29 are directed to an oligonucleotide comprising a molecular interaction site that is present in prokaryotic RNA and in at least one additional prokaryotic RNA, wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular interaction site modulates the expression of said prokaryotic RNA and wherein the binding of said molecule to said molecular interaction site does not modulate translation of said RNA. The specification does not provide a guidance to show that binding of one molecule to a molecular interaction site of a prokaryotic RNA only can modulate the expression of said prokaryotic RNA but can not modulate translation of said RNA. Since it is known in the art that DNA transcripts to RNA and then the RNA translate to protein (see TEXTBOOK of Biochemistry with clinical correlations, Third Edition, 1992, pages 622), a factor that affects a RNA expression must affect the RNA translation. In view if claims 27-29, it is unclear why binding of one molecule to a molecular interaction site of a prokaryotic RNA, which can modulate the expression of said prokaryotic RNA, can not modulate translation of said RNA.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. These undue experimentation at least includes to test whether there is a molecular interaction site of a prokaryotic RNA that can modulate the expression of said prokaryotic RNA but can not modulate translation of said RNA.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 35-40, 43-57, and 59-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Molecular Biology of The Cell, Third Edition (pages 466, 1994).

Regarding claims 35, 39, 40, 51, 52, 56, 57, and 67, since Molecular Biology of The Cell, Third Edition teach poly-A-binding proteins and it is known that mRNA from eukaryotic cells has a polyA tail that can affect mRNA stability (ie., modulating the expression of mRNA) (see page 466), polyA tail is a molecular interaction site as recited in claims 35, 39, 40, 51, and 52, 56, 57, and 67. Although the molecular interaction site taught by Molecular Biology of The Cell, Third Edition is not identified by the method recited in claims 35, 51, 52, and 67, it is well established that even though product-by process claims are limited by and defined by the process, the determination of the patentability of the product is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product is made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Regarding claims 36-38, 43-50, 53-55, and 59-66, since these claims are product-by process claims and are dependent on claims 35 and 52, they are also rejected.

Therefore, Molecular Biology of The Cell, Third Edition teaches all limitations recited in claims 35-40, 43-57, and 59-67.

19. Claims 27, 35-38, 41, 43-55, and 58-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Zubay (Biochemistry, third edition, pages 817 and 818, 1993).

Regarding claims 27, 35, 41, 51, 52, 58, and 67, since Zubay teaches that RNase P binds to tRNA and specially cuts 5' to tRNA-like structure in E. Coli (see pages 817 and 818), tRNA has a molecular interaction site for RNase P as recited in claims 27, 35, 41, 51, and 52, 58, and 67 because RNase P modulates the expression of tRNA by cutting tRNA. Although the molecular interaction site taught by Zubay is not identified by the method recited in claims 35, 51, 52, and 67, it is well established that even though product-by process claims are limited by and defined by the process, the determination of the patentability of the product is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product is made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Regarding claims 36-38, 43-50, 53-55, and 59-66, since these claims are product-by process claims and are dependent on claims 35 and 52, they are also rejected.

Therefore, Zubay teaches all limitations recited in claims 27, 35-38, 41, 43-55, and 58-67.

Conclusion

11. No claim is allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
PSA
December 29, 2003